Oral Maxillofac Surg (2010) 14:227–232
DOI 10.1007/s10006-010-0227-8

ORIGINAL ARTICLE

Aggressive fibromatosis of the head and neck: a new classification based on a literature review over 40 years (1968–2008)

Astrid L. Kruse · Heinz T. Luebbers · Klaus W. Grätz · Joachim A. Obwegeser

Published online: 21 April 2010

Abstract
Background Fibromatosis is an aggressive fibrous tumor of unknown etiology that is, in some cases, lethal. Until now, there has been no particular classification for the head and neck. Therefore, the aim of the present study was to review the current literature in order to propose a new classification for future studies.
Methods An evidence-based literature review was conducted from the last 40 years regarding aggressive fibromatosis in the head and neck. Studies that summarized patients' data without including individual data were excluded.
Results Between 1968 and 2008, 179 cases with aggressive fibromatosis of the head and neck were published. The male to female ratio was 91 to 82 with a mean age of 16.87 years, and 57.32% of the described cases that involved the head and neck were found in patients under 11 years. The most common localization was the mandible, followed by the neck. All together, 143 patients were followed up, and in 43 (30.07%), a recurrence was seen.
Conclusion No clear prognostic factors for recurrence (age, sex, or localization) were observed. A new classification with regard to hormone receptors and bone involvement could improve the understanding of risk factors and thereby assist in future studies.

Keywords Aggressive fibromatosis · Head and neck · Fibrous proliferative disorders

A. L. Kruse (✉) · H. T. Luebbers · K. W. Grätz · J. A. Obwegeser
Department of Craniomaxillofacial and Oral Surgery,
University of Zurich,
Frauenklinikstr. 24,
CH-8091 Zurich, Switzerland
e-mail: astridkruse@gmx.ch

Introduction

Fibromatosis is an aggressive fibrous tumor that is characterized by local invasiveness and a high recurrence rate. Erosion and invasion of the bone may occur, but metastasizing has not been described. This entity belongs to a group of fibrous proliferative disorders including plantar fibromatosis (Dupuytren), penile fibromatosis (Peyronie disease), palmar fibromatosis (Ledderhose disease), abdominal fibromatosis, and intra-abdominal fibromatosis [1].

Only 12% of extra-abdominal fibromatoses arise in the head and neck region. One of the largest series of head and neck involvements was published by Conley et al. in 1966 [2]. This tumor seems to be more aggressive in the head and neck than those arising from the abdominal wall. One reason could be the restricted anatomy, with its vital vascular, neural structures contributing to the severity of the clinical manifestation, as well as to the recurrence rate following attempts at surgical removal.

However, two main classifications for fibromatosis have been introduced, one by Allen in 1977 [3] (Table 1) and one by Enziger and Weiss in 1995 [1], which is a classification with two subdivisions: superficial (fascial) and deep (musculoaponeurotic) fibromatosis.

However, no classification has been published so far dealing with fibromatosis of the head and neck. Therefore, the aim of the present study was to determine the common features of and prognostic factors for this uncommon, but aggressive, disease in the head and neck, with the intent to propose a new classification.

Table 1 Classification by Allen [3]

Classification by Allen [3]
Extra-abdominal
Abdominal wall desmoids
Intra-abdominal desmoids
Multiple desmoids
Desmoids in Gardner`s syndrome

Material and method

For the literature review, a search strategy was devised in consultation with a senior librarian at the University of Zurich in which electronic databases (Medline and Cochrane) were searched using a set of predetermined keywords. The search strategy was initially developed and implemented for PubMed but was revised appropriately to suit the other databases. No restriction was placed on the language of publication. Studies that summarized patients' data without including individual data were excluded.

The citations retrieved from each database were exported into EndNote, which is bibliometric management software. Duplicates were discarded. The titles and abstracts were screened, and hard copies of all potentially relevant articles were retrieved. Their reference lists were manually searched for any related articles.

Results

Between 1968 and 2008, 179 cases were published dealing with aggressive fibromatosis of the head and neck. The male/female ratio was almost 1:1 (91–82) with a mean age of 16.87 years (Fig. 1). However, 57.32% of the described cases with head and neck involvement were found in patients under 11 years of age. The most common localization was the mandible, followed by the neck, but an exact localization is difficult to define because of the differentiation in the case reports between mandible, submandibular, and neck (Fig. 2).

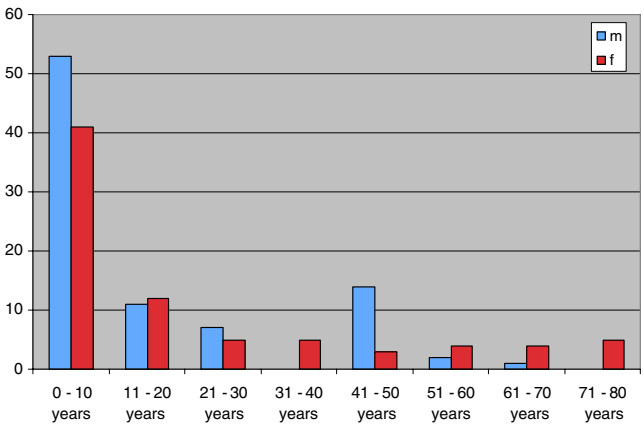

Fig. 1 Age distribution

Concerning therapy, several strategies have been reported (Fig. 3). In six cases, tamoxifen therapy—because of positive hormone receptors—has been admitted. Concerning recurrence rate, an exact comparison is impossible due to different follow-up times.

A total of 143 patients were followed up, and in 43 cases (30.07%), a recurrence was seen (Fig. 4), but no correlation with localization was detected. In one patient, a transformation into a fibrosarcoma occurred [4], and another publication discussed the development of a fibrosarcoma [5]. Invasion of nerves and blood vessels was never reported.

Discussion

The pathogenesis of these nonencapsulated lesions is still unknown; they take their origin from fascia, periosteum, or musculocaponeuroses [6]. Desmoid fibromatosis, also called aggressive fibromatosis and musculoaponeurotic fibromatosis, can be associated with polyposis coli, colonic adenocarcinoma, epidermoid cysts, and osteomas; in a very few cases, it can be fatal [3].

Some authors have implicated trauma [7] or genetic and endocrine factors in the development of these lesions [8]. The terminology was first defined by Stout in 1954 [9]. Several terms have been used in the literature in order to describe this entity: desmoid tumor, desmona, and non-metastasizing fibrosarcoma [10].

Differential diagnoses include fibroma, keloid, fibromatosis, fibrosarcoma, and myositis proliferans. Concerning myositis proliferans, both diseases present infiltration of muscle and in the ligament tissue, draught of fish pattern, but myositis proliferans grows faster, presenting more mitoses, and contrary to aggressive fibromatosis, a pleomorphic cell overview [5]. Table 2 presents an overview of the immunohistochemical profiles of benign spindle cell lesions.

Because of the aggressive growth pattern and high cell concentration, this classification is based on differentiation between children and adults, but our review does not support the conclusion that in children, the tumor is more aggressive than in adults.

Concerning incidence, only very few data are available. The estimated incidence in the general population is 2–4/1,000,000/year [11]. No significant racial or ethnic distribution is reported. In children, a fibromatosis incidence of 2.2% is mentioned [12]. A manifestation in the head and

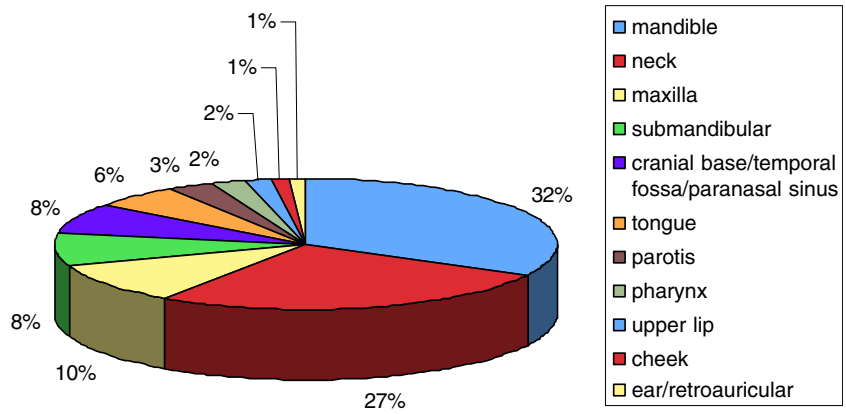

Fig. 2 Distribution of localization

neck is reported in 12% of all cases [7]. Inguinal fibroblastic and myofibroblastic tumors are present in about 12% of soft tissue tumors, and 76% are benign. In 27% of cases, the topography site is the head and side of the neck, and 71% occur in the first decade of life [13]. Other authors estimate that 34% of all fibromatoses occur in the head and neck [14]. The mastoid region is described by some authors as one of the most common localizations in the head and neck [7, 15]. This was not supported by our review, in which the preferred sites in the head and neck region were mandible and neck.

Tumors in the oral cavity and paranasal sinus seem to be more aggressive and lethal than those on other sides [7]. This fact emphasizes the need for a separate classification for this entity. Lakhan et al. reported that approximately 0.03% of all neoplasms are desmoid tumors and that they constitute less than 3% of all soft tissue tumors [16]. An identification of clonal chromosomal changes has been reported in a significant fraction of cases [17]. Trisomie 8 and 20 in desmoid tumors have been discussed [18].

Concerning therapy options, several proposals have been reported (Table 3), but most authors advocate a direct surgical approach; in cases of unresectable tumors because of anatomical limits in order to reduce tumor size, some authors have suggested chemotherapy. Concerning radiotherapy, only very few results have been published. Spear et al. and Posner et al. showed in their studies that radiotherapy, added to surgery with residual disease or to surgery for recurrent disease, led to significant improvement in local control [19, 20], but there is still controversy concerning the dose, particularly in growing children because of possible long-time complications. In their study, Spear et al. reported a difference in local control for doses <50 Gy (36% versus >50 Gy (88%)) [19]. Chalmers et al. implied some interesting points concerning the effect of radiotherapy without surgery [21]. On the one hand, surgery and trauma can provide an impetus for tumor development; therefore, avoidance of surgery with only radiotherapy could lead to improvement. On the other hand, radiotherapy itself could change the tumor behavior. If surgery is performed, controversy still surrounds the recommendation for surgical margins: Plukker et al. advocate 3-cm margins in adults [22]. Recurrence is described more frequently in young patients [3], but our results do not support this theory.

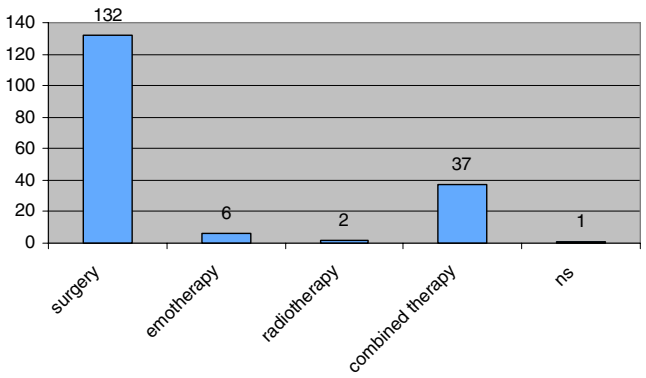

Fig. 3 Distribution of therapy

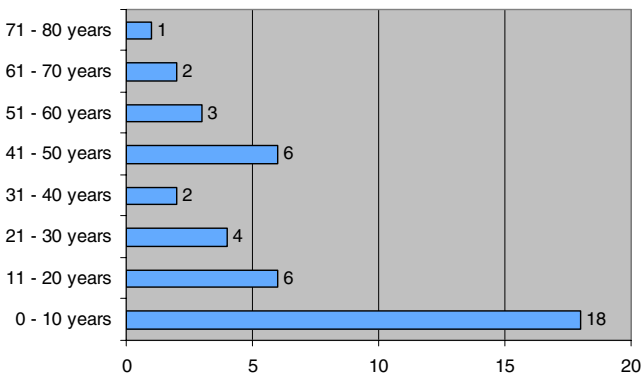

Fig. 4 Age distribution of recurrence

Table 2 Immunohistochemical profiles of fibromatosis and other benign spindle cell lesions [35, 36]

	Vimentin	Actin	S100	Desmin
Fibromatosis	+	−	−	−
Infantile myofibromatosis	+	+	−	−
Neurofibroma	+	−	+	−
Leiomyoma	+	+	−	+
Nodular fasciitis	+	+	−	−
Fibrous histiocytoma	+	+/−	−	−

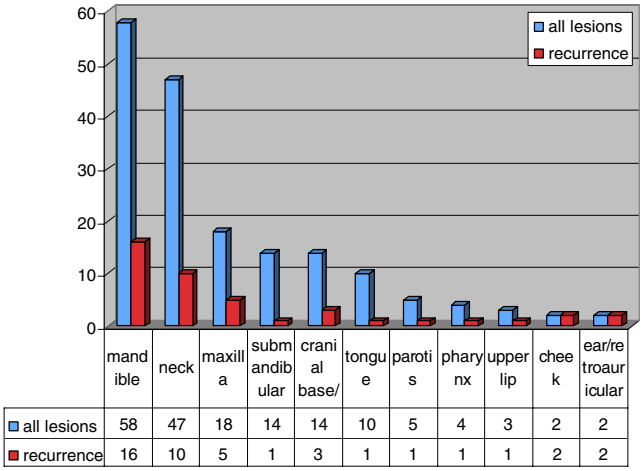

Fig. 5 Distribution of recurrence in relation to localization

One concern in radiotherapy for children is its negative influence on growth, leading to possible deformities.

The possibility of non-surgical treatment is interesting in particular for tumors localized in anatomically difficult structures that need to be preserved as much as possible, e. g., the sinuses. On the other hand, one has to keep in mind the potential toxicity associated with the systemic application of chemotherapy. Surgical resection that results in tumor-free margins and a function-preserving approach are the goals.

Therefore, some authors advocate an estrogen receptor test on the tissue sample in order to provide tamoxifen therapy because spontaneous regression has been observed in the menarche and menophase [23]. One reason seems to be the ability of antiestrogen compounds in vitro to stimulate the secretion of transforming growth factor beta (TGFb) by stromal fibroblasts, leading to inhibiting the growth of surrounding epithelial cells. Benson and Baum [24] hypothesize that in aggressive fibromatosis, the tissue may consist of immature fibroblasts with a fetal phenotype characterized by a negative growth response to TGFb, but the short and long-term toxicity to children (with regard to growth, puberty) resulting from this hormonal therapy must be considered. In women that have been treated with tamoxifen for breast cancer, an increased probability for incidence of endometrial carcinomas is discussed.

In recent times, some authors have advocated another therapy option with interferon alpha for disease stabilization because IFN type I seems to be a positive regulator of neoplastic growth [25, 26]. Another therapy option could be tyrosine kinase inhibitor imatinib due to tumor expression of activated receptor tyrosine kinase c-kit and/or platelet-derived growth factor receptor alpha [27].

Controversy also surrounds radiotherapy. Some authors advocate this therapy option [28], whereas others doubt the effect, in particular at high doses because of side effects. The problem concerning all these therapy options seems to be the lack of experience in using them for head and neck fibromatosis; it seems to be more common to use these strategies in intra-abdominal manifestations where resections can be difficult because of the diffuse infiltration.

Some authors prefer a radical neck dissection for all neck fibromatoses in order to reduce recurrence rates by 33% through aggressive surgery [29], but since aggressive fibromatosis do not metastasize and because the recurrence rate is higher in young patients, one should be careful with the indication for a radical neck dissection.

The only factor for recurrence-free follow-up seems to be negative margins [16, 30, 31]. On the other hand, some authors claim that recurrence seems to be independent of the margin status [32, 33], and a margin of less than 1 mm did not adversely affect outcome when compared with more generous margins.

Our results show that the probability for recurrence seems to be independent of age or localization (Fig. 5).

Table 3 Overview of different therapy options

Surgery
Chemotherapy (vincristine/actinomycin, cyclophosphamide, or methotrexate/vinblastine) [37]
Hyperthermia
Hormone therapy (antiestrogen) [38]
NSAR therapy [38]
Radiation
Selective tyrosine kinase inhibitor and alpha-interferon [39]
Combined therapy

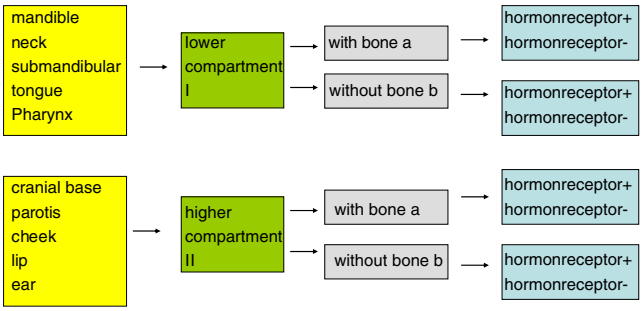

Fig. 6 Proposal for new classification

Other researchers have included as prognostic factors an age of less than 18 years, recurrent disease, and treatment with surgery alone [19]. Concerning localization, Scougall et al. [34] showed that there are no differences in the outcome between children and adults.

Because of missing correlations among the localization, age, and recurrence rates, we propose a new classification for this entity in order to evaluate further cases (Fig. 6).

Conclusion

No clear prognostic factors for recurrence (age, sex, or localization) were observed. A new classification with regard to hormone receptors and bone involvement could improve the understanding of risk factors clinically and for future studies.

Acknowledgments The authors would like to thank Hildegard Eschle, senior librarian of the Dental School at the University Zurich, for helping with the literature research.

Conflict of interests The authors declare that they have no conflict of interest.

References

1. Enzinger FM, Weiss SW (1995) Fibromatosis. In: Enzinger FM, Weiss SW (eds) Soft tissue tumours. St. Louis, Mosby, pp 201–229
2. Conley J, Healey WV, Stout AP (1966) Fibromatosis of the head and neck. Am J Surg 112(4):609–614
3. Allen PW (1977) The fibromatoses: a clinicopathologic classification based on 140 cases. Am J Surg Pathol 1(3):255–270
4. De Santis D (1998) Fibromatosis of the mandible: case report and review of previous publications. Br J Oral Maxillofac Surg 36 (5):384–388
5. Fritzmeier F, Kronsbein H, Draf W (1981) Diagnosis and therapy of fibromatosis in head and neck region (author's transl). HNO 29 (4):105–111
6. Fowler CB, Hartman KS, Brannon RB (1994) Fibromatosis of the oral and paraoral region. Oral Surg Oral Med Oral Pathol 77 (4):373–386
7. Tostevin PM, Wyatt M, Hosni A (2000) Six cases of fibromatosis of the head and neck in children. Int J Pediatr Otorhinolaryngol 53 (3):235–244
8. Hayry P et al (1982) The desmoid tumor. III. A biochemical and genetic analysis. Am J Clin Pathol 77(6):681–685
9. Stout AP (1954) Juvenile fibromatoses. Cancer 7(5):953–978
10. Stout AP (1962) Fibrosarcoma in infants and children. Cancer 15:1028–1040
11. Reitamo JJ et al (1982) The desmoid tumor. I. Incidence, sex-, age- and anatomical distribution in the Finnish population. Am J Clin Pathol 77(6):665–673
12. Humar A, Chou S, Carpenter B (1993) Fibromatosis in infancy and childhood: the spectrum. J Pediatr Surg 28 (11):1446–1450
13. Styczynski J, Lasek W, Wysocki M (2005) Calcified fibromatosis of the neck in 4-year old girl: rapid growth, rapid therapy. Int J Pediatr Otorhinolaryngol 69(6):847–852
14. Bhaskar AR et al (1994) Large myofascial fibromatosis involving the shoulder girdle. J Postgrad Med 40(4):225–227
15. Kingston CA et al (2002) Imaging of desmoid fibromatosis in pediatric patients. AJR Am J Roentgenol 178(1):191–199
16. Lakhan SE, Eager RM, Harle L (2008) Aggressive juvenile fibromatosis of the paranasal sinuses: case report and brief review. J Hematol Oncol 1:3
17. De Wever I et al (2000) Cytogenetic, clinical, and morphologic correlations in 78 cases of fibromatosis: a report from the CHAMP Study Group. Chromosomes and morphology. Mod Path 13(10):1080–1085
18. Qi H et al (1996) Trisomies 8 and 20 in desmoid tumors. Cancer Genet Cytogenet 92(2):147–149
19. Spear MA et al (1998) Individualizing management of aggressive fibromatoses. Int J Radiat Oncol Biol Phys 40 (3):637–645
20. Posner MC et al (1989) The desmoid tumor. Not a benign disease. Arch Surg 124(2):191–196
21. Chalmers AJ, Gillham CM, Plowman PN (2001) Nuchal aggressive fibromatosis in childhood: two instructive case reports. Clin Oncol (R Coll Radiol) 13(5):378–383
22. Plukker JT et al (1995) Aggressive fibromatosis (non-familial desmoid tumour): therapeutic problems and the role of adjuvant radiotherapy. Br J Surg 82(4):510–514
23. Masson JK, Soule EH (1966) Desmoid tumors of the head and neck. Am J Surg 112(4):615–622
24. Benson JR, Baum M (1993) Breast cancer, desmoid tumours, and familial adenomatous polyposis—a unifying hypothesis. Lancet 342(8875):848–850
25. Leithner A et al (2000) Treatment of extra-abdominal desmoid tumors with interferon-alpha with or without tretinoin. J Surg Oncol 73(1):21–25
26. Raguse JD et al (2004) Interferon-induced remission of rapidly growing aggressive fibromatosis in the temporal fossa. Int J Oral Maxillofac Surg 33(6):606–609
27. Heinrich MC et al (2006) Clinical and molecular studies of the effect of imatinib on advanced aggressive fibromatosis (desmoid tumor). J Clin Oncol 24(7):1195–1203
28. Park HC et al (2003) Radiation treatment for aggressive fibromatosis: findings from observed patterns of local failure. Oncology 64(4):346–352
29. Hunt RT, Morgan HC, Ackerman LV (1960) Principles in the management of extra-abdominal desmoids. Cancer 13:825–836
30. Faulkner LB et al (1995) Pediatric desmoid tumor: retrospective analysis of 63 cases. J Clin Oncol 13(11):2813–2818
31. Buitendijk S et al (2005) Pediatric aggressive fibromatosis: a retrospective analysis of 13 patients and review of literature. Cancer 104(5):1090–1099

32. Gronchi A et al (2003) Quality of surgery and outcome in extra-abdominal aggressive fibromatosis: a series of patients surgically treated at a single institution. J Clin Oncol 21(7):1390–1397
33. Reitamo JJ (1983) The desmoid tumor. IV. Choice of treatment, results, and complications. Arch Surg 118(11):1318–1322
34. Scougall P et al (1987) Desmoid tumors in childhood. Orthop Rev 16(7):481–488
35. Gebert C et al (2007) Expression of beta-catenin and p53 are prognostic factors in deep aggressive fibromatosis. Histopathology 50(4):491–497
36. Turner MS, Goldsmith JD (2009) Best practices in diagnostic immunohistochemistry: spindle cell neoplasms of the gastrointestinal tract. Arch Pathol Lab Med 133(9):1370–1374
37. Azzarelli A et al (2001) Low-dose chemotherapy with methotrexate and vinblastine for patients with advanced aggressive fibromatosis. Cancer 92(5):1259–1264
38. Lackner H et al (1997) Noncytotoxic drug therapy in children with unresectable desmoid tumors. Cancer 80(2):334–340
39. Mace J et al (2002) Response of extraabdominal desmoid tumors to therapy with imatinib mesylate. Cancer 95(11):2373–2379